

What is claimed is:

1. An isolated nucleic acid molecule comprising a nucleotide sequence that
5 encodes a polypeptide comprising an amino acid sequence homologous to sequences
selected from the group consisting of: SEQ ID NO:24 to SEQ ID NO:27, and SEQ ID
NO:46, and fragments thereof; said nucleic acid molecule encoding at least a portion
of nGPCR-x.
- 10 2. The isolated nucleic acid molecule of claim 1 comprising a sequence that
encodes a polypeptide comprising a sequence selected from the group consisting of
SEQ ID NO:24 to SEQ ID NO:27, and SEQ ID NO:46, and fragments thereof.
- 15 3. The isolated nucleic acid molecule of claim 1 comprising a sequence
homologous to a sequence selected from the group consisting of SEQ ID NO:11 to
SEQ ID NO:13, and SEQ ID NO:45, and fragments thereof.
- 20 4. The isolated nucleic acid molecule of claim 1 comprising a sequence selected
from the group of sequences consisting of SEQ ID NO:11 to SEQ ID NO:13, and
SEQ ID NO:45, and fragments thereof.
- 25 5. The isolated nucleic acid molecule of claim 4 comprising a sequence selected
from the group of sequences consisting of SEQ ID NO:11 to SEQ ID NO:13, and
SEQ ID NO:45.
6. The isolated nucleic acid molecule of claim 4 wherein said nucleotide
sequence is selected from the group consisting of: SEQ ID NO:12 and SEQ ID
NO:45.
- 30 7. The isolated nucleic acid molecule of claim 1 wherein said nucleic acid
molecule is DNA.
8. The isolated nucleic acid molecule of claim 1 wherein said nucleic acid
molecule is RNA.
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9. An expression vector comprising a nucleic acid molecule of any one of claims 1 to 5.
10. The expression vector of claim 9 wherein said nucleic acid molecule comprises a sequence selected from the group of sequences consisting of SEQ ID NO:11 to SEQ ID NO:13, and SEQ ID NO:45.
11. The expression vector of claim 9 wherein said nucleic acid molecule comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:12 and SEQ ID NO:45.
12. The expression vector of claim 9 wherein said vector is a plasmid.
13. The expression vector of claim 9 wherein said vector is a viral particle.
14. The expression vector of claim 13 wherein said vector is selected from the group consisting of adenoviruses, baculoviruses, parvoviruses, herpesviruses, poxviruses, adeno-associated viruses, Semliki Forest viruses, vaccinia viruses, and retroviruses.
15. The expression vector of claim 9 wherein said nucleic acid molecule is operably connected to a promoter selected from the group consisting of simian virus 40, mouse mammary tumor virus, long terminal repeat of human immunodeficiency virus, maloney virus, cytomegalovirus immediate early promoter, Epstein Barr virus, rous sarcoma virus, human actin, human myosin, human hemoglobin, human muscle creatine, and human metallothionein.
16. A host cell transformed with an expression vector of claim 9.
17. The transformed host cell of claim 16 wherein said cell is a bacterial cell.
18. The transformed host cell of claim 17 wherein said bacterial cell is *E. coli*.
19. The transformed host cell of claim 16 wherein said cell is yeast.

20. The transformed host cell of claim 19 wherein said yeast is *S. cerevisiae*.
21. The transformed host cell of claim 16 wherein said cell is an insect cell.
22. The transformed host cell of claim 21 wherein said insect cell is *S. frugiperda*.
23. The transformed host cell of claim 16 wherein said cell is a mammalian cell.
24. The transformed host cell of claim 23 wherein mammalian cell is selected from the group consisting of chinese hamster ovary cells, HeLa cells, African green monkey kidney cells, human 293 cells, and murine 3T3 fibroblasts.
25. An isolated nucleic acid molecule comprising a nucleotide sequence complementary to at least a portion of a sequence selected from the group of sequences consisting of SEQ ID NO:11 to SEQ ID NO:13, and SEQ ID NO:45, said portion comprising at least 10 nucleotides.
26. The nucleic acid molecule of claim 25 wherein said molecule is an antisense oligonucleotide directed to a region of a sequence selected from the group of sequences consisting of SEQ ID NO:11 to SEQ ID NO:13, and SEQ ID NO:45.
27. The nucleic acid molecule of claim 26 wherein said oligonucleotide is directed to a regulatory region of a sequence selected from the group of sequences consisting of SEQ ID NO:11 to SEQ ID NO:13, and SEQ ID NO:45.
28. The nucleic acid molecule of claim 25 wherein said molecule is an antisense oligonucleotide directed to a region of nucleotide sequence selected from the group consisting of: SEQ ID NO:12, and SEQ ID NO:45.
29. A composition comprising a nucleic acid molecule of any one of claims 1 to 5 or 25 and an acceptable carrier or diluent.

30. A composition comprising a recombinant expression vector of claim 9 and an acceptable carrier or diluent.

31. A method of producing a polypeptide that comprises a sequence selected from the group of sequences consisting SEQ ID NO:24 to SEQ ID NO:27, and SEQ ID NO:46, and homologs and fragments thereof, said method comprising the steps of:

- a) introducing a recombinant expression vector of claim 10 into a compatible host cell;
- b) growing said host cell under conditions for expression of said polypeptide; and
- c) recovering said polypeptide.

32. The method of claim 31 wherein said host cell is lysed and said polypeptide is recovered from the lysate of said host cell.

33. The method of claim 31 wherein said polypeptide is recovered by purifying the culture medium without lysing said host cell.

34. An isolated polypeptide encoded by a nucleic acid molecule of claim 1.

35. The polypeptide of claim 34 wherein said polypeptide comprises a sequence selected from the group of sequences consisting of SEQ ID NO:24 to SEQ ID NO:27, and SEQ ID NO:46.

36. The polypeptide of claim 34 wherein said polypeptide comprises an amino acid sequence homologous to a sequence selected from the group of sequences consisting of SEQ ID NO:24 to SEQ ID NO:27, and SEQ ID NO:46.

37. The polypeptide of claim 34 wherein said sequence homologous to a sequence selected from the group of sequences consisting of SEQ ID NO:24 to SEQ ID NO:27, and SEQ ID NO:46 comprises at least one conservative amino acid substitution compared to the sequences in the group of sequences consisting of SEQ ID NO:24 to SEQ ID NO:27, and SEQ ID NO:46.

38. The polypeptide of claim 34 wherein said polypeptide comprises a fragment of a polypeptide with a sequence selected from the group of sequences consisting of SEQ ID NO:24 to SEQ ID NO:27, and SEQ ID NO:46.

5 39. The polypeptide of claim 34 wherein said polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:25 and SEQ ID NO:46.

10 40. A composition comprising a polypeptide of claim 34 and an acceptable carrier or diluent.

41. An isolated antibody which binds to an epitope on a polypeptide of claim 34.

15 42. The antibody of claim 41 wherein said antibody is a monoclonal antibody.

43. A composition comprising an antibody of claim 41 and an acceptable carrier or diluent.

20 44. A method of inducing an immune response in a mammal against a polypeptide of claim 34 comprising administering to said mammal an amount of said polypeptide sufficient to induce said immune response.

45. A method for identifying a compound which binds nGPCR-x comprising the steps of:

- 25 a) contacting nGPCR-x with a compound; and
 b) determining whether said compound binds nGPCR-x.

46. The method of claim 45 wherein the nGPCR-x comprises an amino acid sequence selected from the group consisting of SEQ ID NO:25 and SEQ ID NO:46.

30 47. The method of claim 45 wherein binding of said compound to nGPCR-x is determined by a protein binding assay.

48. The method of claim 45 wherein said protein binding assay is selected from the group consisting of a gel-shift assay, Western blot, radiolabeled competition assay, phage-based expression cloning, co-fractionation by chromatography, co-precipitation, cross linking, interaction trap/two-hybrid analysis, southwestern analysis, and ELISA.
49. A compound identified by the method of claim 45.
50. A method for identifying a compound which binds a nucleic acid molecule encoding nGPCR-x comprising the steps of:
- a) contacting said nucleic acid molecule encoding nGPCR-x with a compound; and
 - b) determining whether said compound binds said nucleic acid molecule.
51. The method of claim 50 wherein binding is determined by a gel-shift assay.
52. A compound identified by the method of claim 50.
53. A method for identifying a compound which modulates the activity of nGPCR-x comprising the steps of:
- a) contacting nGPCR-x with a compound; and
 - b) determining whether nGPCR-x activity has been modulated.
54. The method of claim 53 wherein the nGPCR-x comprises an amino acid sequence selected from the group consisting of SEQ ID NO:25 and SEQ ID NO:46.
55. The method of claim 53 wherein said activity is neuropeptide binding.
56. The method of claim 53 wherein said activity is neuropeptide signaling.
57. A compound identified by the method of claim 53.

58. A method of identifying an animal homolog of nGPCR-x comprising the steps:

- a) comparing the nucleic acid sequences of the animal with a sequence selected from the group of sequence consisting of SEQ ID NO:11 to SEQ ID NO:13, and SEQ ID NO:45, and portions thereof, said portions being at least 10 nucleotides; and
- b) identifying nucleic acid sequences of the animal that are homologous to said sequence selected from the group sequence consisting of SEQ ID NO:11 to SEQ ID NO:13, and SEQ ID NO:45, and portions thereof.

59. The method of claim 58 wherein comparing the nucleic acid sequences of the animal with a sequence selected from the group of sequences consisting of SEQ ID NO:11 to SEQ ID NO:13, and SEQ ID NO:45, and portions thereof, said portions being at least 10 nucleotides, is performed by DNA hybridization.

60. The method of claim 58 wherein comparing the nucleic acid sequences of the animal with a sequence selected from the group of sequences consisting of SEQ ID NO:11 to SEQ ID NO:13, and SEQ ID NO:45, and portions thereof, said portions being at least 10 nucleotides, is performed by computer homology search.

61. A method of screening a human subject to diagnose a disorder affecting the brain or genetic predisposition therefor, comprising the steps of:

(a) assaying nucleic acid of a human subject to determine a presence or an absence of a mutation altering an amino acid sequence, expression, or biological activity of at least one nGPCR that is expressed in the brain, wherein the nGPCR comprises an amino acid sequence selected from the group consisting of: SEQ ID NO:12, and SEQ ID NO:45, and allelic variants thereof, and wherein the nucleic acid corresponds to a gene encoding the nGPCR; and

(b) diagnosing the disorder or predisposition from the presence or absence of said mutation, wherein the presence of a mutation altering the amino acid sequence, expression, or biological activity of the nGPCR in the nucleic acid correlates with an increased risk of developing the disorder.

62. A method according to claim 61, wherein the nGPCR is nGPCR-1002 comprising an amino acid sequence set forth in SEQ ID NO:46 or an allelic variant thereof.

5 63. A method according to claim 61, wherein the nGPCR is nGPCR-1007 comprising an amino acid sequence set forth in SEQ ID NO:25 or an allelic variant thereof.

10 64. A method according to claim 61, wherein the disease is a mental disorder.

65. A method according to claim 61, wherein the assaying step comprises at least one procedure selected from the group consisting of:

- 15 a) comparing nucleotide sequences from the human subject and reference sequences and determining a difference of either
at least a nucleotide of at least one codon
between the nucleotide sequences from the human subject that encodes an nGPCR-1002 allele and an nGPCR-1002 reference sequence, or
at least a nucleotide of at least one codon
between the nucleotide sequences from the human subject that encodes an nGPCR-1007 allele and an nGPCR-1007 reference sequence;
- 20 (b) performing a hybridization assay to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences;
- (c) performing a polynucleotide migration assay to determine
25 whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences; and
- (d) performing a restriction endonuclease digestion to determine
whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences.

30 66. A method according to claim 65 wherein the assaying step comprises: performing a polymerase chain reaction assay to amplify nucleic acid comprising nGPCR-1002 or nGPCR-1007 coding sequence, and determining nucleotide sequence of the amplified nucleic acid.

67. A method of screening for an nGPCR-1002 or nGPCR-1007 hereditary mental disorder genotype in a human patient, comprising the steps of:

- (a) providing a biological sample comprising nucleic acid
5 from said patient, said nucleic acid including sequences corresponding to alleles of nGPCR-1002 or nGPCR-1007; and
(b) detecting the presence of one or more mutations in the nGPCR-1002 allele or the nGPCR-1007 allele;

wherein the presence of a mutation in a nGPCR-1002 allele or nGPCR-1007
10 allele is indicative of a hereditary mental disorder genotype.

68. The method according to claim 67 wherein said biological sample is a cell sample.

15 69. The method according to claim 67 wherein said detecting the presence of a mutation comprises sequencing at least a portion of said nucleic acid, said portion comprising at least one codon of said nGPCR-1002 or nGPCR-1007 alleles.

70. The method according to claim 67 wherein said nucleic acid is DNA.

20 71. The method according to claim 67 wherein said nucleic acid is RNA.

72. A kit for screening a human subject to diagnose a mental disorder or a genetic predisposition therefor, comprising, in association:

- 25 (a) an oligonucleotide useful as a probe for identifying polymorphisms in a human nGPCR-1002 gene or a human nGPCR-1007 gene, the oligonucleotide comprising 6-50 nucleotides in a sequence that is identical or complementary to a sequence of a wild type human nGPCR-1002 or nGPCR-1007 gene sequence or nGPCR-1002 or nGPCR-1007 coding sequence, except for one
30 sequence difference selected from the group consisting of a nucleotide addition, a nucleotide deletion, or nucleotide substitution; and

(b) a media packaged with the oligonucleotide, said media containing information for identifying polymorphisms that correlate with mental

disorder or a genetic predisposition therefor, the polymorphisms being identifiable using the oligonucleotide as a probe.

73. A method of identifying a nGPCR allelic variant that correlates with a mental disorder, comprising the steps of:
- (a) providing a biological sample comprising nucleic acid from a human patient diagnosed with a mental disorder, or from the patient's genetic progenitors or progeny;
 - (b) detecting in the nucleic acid the presence of one or more mutations in an nGPCR that is expressed in the brain, wherein the nGPCR comprises an amino acid sequence selected from the group consisting of SEQ ID NO:25, and SEQ ID NO:46, and allelic variants thereof, and wherein the nucleic acid includes sequence corresponding to the gene or genes encoding nGPCR;
- wherein the one or more mutations detected indicates an allelic variant that correlates with a mental disorder.
74. A method according to claim 73, wherein the disorder is a mental disorder, and wherein the at least one nGPCR is nGPCR-1002, nGPCR-1007, or an allelic variant thereof.
75. A purified and isolated polynucleotide comprising a nucleotide sequence encoding a nGPCR-1002 or nGPCR-1007 allelic variant identified according to claim 74.
76. A host cell transformed or transfected with a polynucleotide according to claim 75 or with a vector comprising the polynucleotide.
77. A purified polynucleotide comprising a nucleotide sequence encoding nGPCR-1002 or nGPCR-1007 of a human with a mental disorder;
- wherein said polynucleotide hybridizes to the complement of SEQ ID NO:12 or of SEQ ID NO:45 under the following hybridization conditions:
- (a) hybridization for 16 hours at 42°C in a hybridization solution comprising 50% formamide, 1% SDS, 1 M NaCl, 10% dextran sulfate and

(b) washing 2 times for 30 minutes at 60°C in a wash solution comprising 0.1x SSC and 1% SDS; and

wherein the polynucleotide that encodes nGPCR-1002 or nGPCR-1007 amino acid sequence of the human differs from SEQ ID NO:25 or SEQ ID NO:46 by at least one residue.

78. A vector comprising a polynucleotide according to claim 77.

79. A host cell that has been transformed or transfected with a polynucleotide according to claim 77 and that expresses the nGPCR-1002 or nGPCR-1007 protein encoded by the polynucleotide.

80. A host cell according to claim 79 that has been co-transfected with a polynucleotide encoding the nGPCR-1002 or nGPCR-1007 amino acid sequence set forth in SEQ ID NO:25 or SEQ ID NO:46 and that expresses the nGPCR-1002 or nGPCR-1007 protein having the amino acid sequence set forth in SEQ ID NO:25 or SEQ ID NO:46.

81. A method for identifying a modulator of biological activity of nGPCR-1002 or nGPCR-1007 comprising the steps of:

- a) contacting a cell according to claim 79 in the presence and in the absence of a putative modulator compound;
- b) measuring nGPCR-1002 or nGPCR-1007 biological activity in the cell;

wherein decreased or increased nGPCR-1002 or nGPCR-1007 biological activity in the presence versus absence of the putative modulator is indicative of a modulator of biological activity.

82. A method to identify compounds useful for the treatment of a mental disorder, said method comprising the steps of:

- (a) contacting a composition comprising nGPCR-1002 with a compound suspected of binding nGPCR-1002 or contacting a composition comprising nGPCR-1007 with a compound suspected of binding nGPCR-1007;

wherein compounds identified as binding nGPCR-1002 or nGPCR-1007 are
5 candidate compounds useful for the treatment of a mental disorder.

10 (a) contacting the binding partner and a composition comprising nGPCR-1002 or nGPCR-1007 in the presence and in the absence of a putative modulator compound;

15 wherein decreased or increased binding between the binding partner and nGPCR-1002 or nGPCR-1007 in the presence of the putative modulator, as compared to binding in the absence of the putative modulator is indicative a modulator compound useful for the treatment of a mental disorder.

85. A method according to claim 84 wherein the composition comprises a cell transformed or transfected with a polynucleotide that encodes nGPCR-1002 or nGPCR-1007.

a) contacting said sample with a polypeptide of claim 1 for a time
30 sufficient to allow said G protein to form a complex with said polypeptide;

c) maintaining said complex under conditions which result in dissociation of said G protein from said polypeptide; and

d) isolating said G protein from said polypeptide.

87. The method of claim 86 wherein said sample comprises an amino acid
sequence selected from the group of sequences consisting of SEQ ID NO:24 to SEQ
5 ID NO:27, and SEQ ID NO:46.

88. The method of claim 86 wherein said polypeptide comprises an amino acid
sequence homologous to a sequence selected from the group of sequences consisting
of SEQ ID NO:24 to SEQ ID NO:27, and SEQ ID NO:46.

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89. The method of claim 86 wherein said polypeptide comprises an amino acid
sequence selected from the group consisting of: SEQ ID NO:25 and SEQ ID NO:46.